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Prevention of Early-onset Neonatal Group B Streptococcal Disease

Green-top Guideline No. 36

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Prevention of Early-onset Neonatal Group B Streptococcal Disease

This is the third edition of this guideline. The second edition was published in 2012 under the same title.

Executive summary

Information for women

What information should women be given about group B streptococcal (GBS) colonisation of the mother and the risk of neonatal infection, during pregnancy and after delivery?

All pregnant women should be provided with an appropriate information leaflet. [*New 2016*] ✓

Antenatal screening

Should all pregnant women be offered bacteriological screening for GBS?

Universal bacteriological screening is not recommended. D

What are the clinical risk factors that affect the risk of GBS disease?

Clinicians should be aware of the clinical risk factors that place women at increased risk of having a baby with early-onset GBS (EOGBS) disease. [*New 2016*] ✓

Should women be offered intrapartum antibiotic prophylaxis (IAP) if GBS was detected in a previous pregnancy, irrespective of carrier status this pregnancy?

Explain to women that the likelihood of maternal GBS carriage in this pregnancy is 50%. Discuss the options of IAP, or bacteriological testing in late pregnancy and then offer of IAP if still positive. [*New 2016*] B

If performed, bacteriological testing should ideally be carried out at 35–37 weeks of gestation or 3–5 weeks prior to the anticipated delivery date, e.g. 32–34 weeks of gestation for women with twins. [*New 2016*] C

Should women with a previous baby affected by GBS disease be offered IAP irrespective of carrier status this pregnancy?

IAP should be offered to women with a previous baby with early- or late-onset GBS disease. D

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What screening tests (if any) should be offered if a woman requests testing for carrier status?

A maternal request is not an indication for bacteriological screening. [*New 2016*] D

Antenatal care

How should GBS bacteriuria in the current pregnancy be managed?

Clinicians should offer IAP to women with GBS bacteriuria identified during the current pregnancy. C

Women with GBS urinary tract infection (growth of greater than 10^5 cfu/ml) during pregnancy should receive appropriate treatment at the time of diagnosis as well as IAP. [*New 2016*] C

Should women be treated before the onset of labour if GBS carriage is detected incidentally earlier in the pregnancy?

Antenatal treatment is not recommended for GBS cultured from a vaginal or rectal swab. C

Should the management differ if the detection of GBS is incidental or following intentional testing, and if so, how?

Where GBS carriage is detected incidentally or by intentional testing, women should be offered IAP. [*New 2016*]

Should being a GBS carrier influence the method of induction? ✓

Method of induction should not vary according to GBS carrier status. [*New 2016*] ✓

Is being a GBS carrier a contraindication to membrane sweeping?

Membrane sweeping is not contraindicated in women who are carriers of GBS. [*New 2016*] D

How should planned caesarean section in women with known GBS colonisation be managed?

Antibiotic prophylaxis specific for GBS is not required for women undergoing planned caesarean section in the absence of labour and with intact membranes. C

Management of term labour (including rupture of membranes) to reduce the risk of EOGBS disease

How should rupture of membranes in a woman at term (37^{+0} weeks of gestation) with known or unknown GBS carrier status be managed?

Women who are known GBS carriers should be offered immediate IAP and induction of labour as soon as reasonably possible. C

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In women where the carrier status is negative or unknown, offer induction of labour immediately or expectant management up to 24 hours. Beyond 24 hours, induction of labour is appropriate. [*New 2016*] A

How should labour in a woman with a temperature of 38°C or greater and without known GBS colonisation be managed?

Women who are pyrexial (38°C or greater) in labour should be offered a broad-spectrum antibiotic regimen which should cover GBS in line with local microbiology sensitivities. C

How should preterm labour be managed in women without known GBS colonisation?

IAP is recommended for women in confirmed preterm labour. [*New 2016*] D

IAP is not recommended for women not in labour and having a preterm planned caesarean section with intact membranes. [*New 2016*] D

Is there a role for polymerase chain reaction or other near-patient testing at the onset of labour?

Polymerase chain reaction or other near-patient testing at the onset of labour is not recommended. [*New 2016*] C

Can GBS-positive women have a water birth?

Birth in a pool is not contraindicated if the woman is a known GBS carrier provided she is offered appropriate IAP. [*New 2016*] D

Management of preterm labour (including rupture of membranes) to reduce the risk of EOGBS disease

Women with preterm rupture of membranes

How should known or unknown GBS carrier status be managed in women with preterm prelabour rupture of membranes?

Bacteriological testing for GBS carriage is not recommended for women with preterm rupture of membranes. IAP should be given once labour is confirmed or induced irrespective of GBS status. [*New 2016*] D

For those with evidence of colonisation in the current pregnancy or in previous pregnancies, the perinatal risks associated with preterm delivery at less than 34^{+0} weeks of gestation are likely to outweigh the risk of perinatal infection. For those at more than 34^{+0} weeks of gestation it may be beneficial to expedite delivery if a woman is a known GBS carrier. [*New 2016*] D

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Bacteriological considerations

What are the appropriate swabs if testing for carrier status is to be undertaken?

When testing for GBS carrier status, a swab should be taken from the lower vagina and the anorectum. A single swab (vagina then anorectum) or two different swabs can be used. [*New 2016*] D

How quickly should the swabs be transported to the laboratory, in what medium and at what temperature?

After collection, swabs should be placed in a non-nutrient transport medium, such as Amies or Stuart. Specimens should be transported and processed as soon as possible. If processing is delayed, specimens should be refrigerated. [*New 2016*] B

What culture medium should be used if testing for GBS carriage is to be undertaken?

Enriched culture medium tests are recommended. The clinician should indicate that the swab is being taken for GBS. [*New 2016*] B

Which antibiotic should be used for IAP?

For women who have agreed to IAP, benzylpenicillin should be administered. Once commenced, treatment should be given regularly until delivery. B

Which antibiotic should be used in women with known or suspected penicillin allergy?

Provided a woman has not had severe allergy to penicillin, a cephalosporin should be used. If there is any evidence of severe allergy to penicillin, vancomycin should be used. [*New 2016*] ✓

How should known GBS colonisation in women who decline IAP be managed?

Women with known GBS colonisation who decline IAP should be advised that the baby should be very closely monitored for 12 hours after birth, and discouraged from seeking very early discharge from the maternity hospital. [*New 2016*] ✓

What are the adverse effects of IAP (maternal anaphylaxis, altered neonatal bowel flora and abnormal child development)?

Clinicians should be aware of the potential adverse effects of IAP. [*New 2016*] C

Should vaginal cleansing be performed in labour and does this differ according to GBS carrier status?

There is no evidence that intrapartum vaginal cleansing will reduce the risk of neonatal GBS disease. C

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How should a newborn baby be managed?

If there have been any concerns about early-onset neonatal infection, what signs should prompt parents and carers to seek medical advice?

Parents and carers should seek urgent medical advice if they are concerned that the baby: D

- **is showing abnormal behaviour (for example, inconsolable crying or listlessness), or**
- **is unusually floppy, or**
- **has developed difficulties with feeding or with tolerating feeds, or**
- **has an abnormal temperature unexplained by environmental factors (lower than 36°C or higher than 38°C), or**
- **has rapid breathing, or**
- **has a change in skin colour. [*New 2016*]**

How should term babies whose mothers have received adequate IAP be managed?

Term babies who are clinically well at birth and whose mothers have received IAP for prevention of EOGBS disease more than 4 hours before delivery do not require special observation. [*New 2016*] ✓

The babies of women who have received broad-spectrum antibiotics during labour for indications other than GBS prophylaxis may require investigation and treatment as per the NICE clinical guideline on early-onset neonatal infection. [*New 2016*] ✓

How should well babies at risk of EOGBS disease whose mothers have not received adequate IAP be monitored?

Well babies should be evaluated at birth for clinical indicators of neonatal infection and have their vital signs checked at 0, 1 and 2 hours, and then 2 hourly until 12 hours. [*New 2016*] ✓

Should postnatal antibiotic prophylaxis be given to low-risk term babies?

Postnatal antibiotic prophylaxis is not recommended for asymptomatic term infants without known antenatal risk factors. C

How should a baby with clinical signs of EOGBS disease be managed?

Babies with clinical signs of EOGBS disease should be treated with penicillin and gentamicin within an hour of the decision to treat. [*New 2016*] ✓

How should the baby of a mother who has had a previous baby with GBS disease be managed?

Babies should be evaluated at birth for clinical indicators of neonatal infection and have their vital signs checked at 0, 1 and 2 hours, and then 2 hourly until 12 hours. [*New 2016*] ✓

What advice should be given to women regarding breastfeeding?

Breastfeeding should be encouraged irrespective of GBS status. [*New 2016*] ✓

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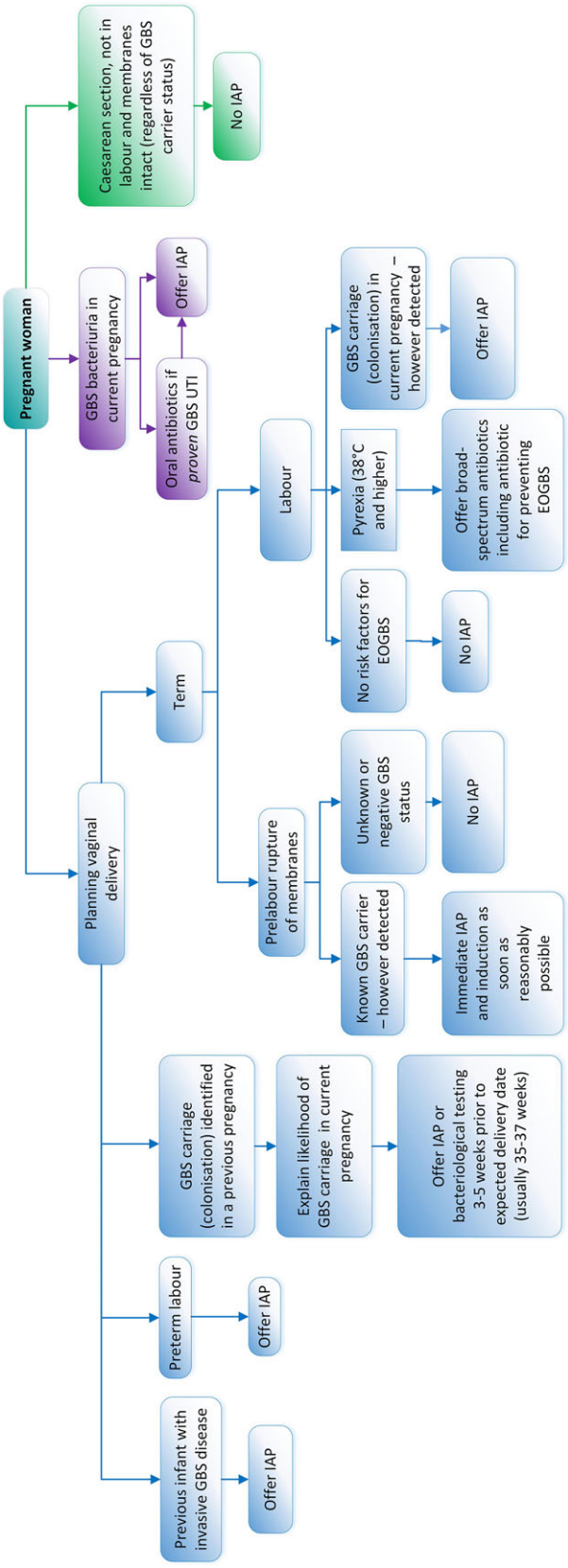
Pathway of care



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1. Purpose and scope

The purpose of this guideline is to provide guidance for obstetricians, midwives and neonatologists on the prevention of early-onset neonatal group B streptococcal (EOGBS) disease and the information to be provided to women, their partners and family. Prevention of late-onset group B streptococcal (GBS) disease and treatment of established GBS disease is not considered beyond initial antibiotic therapy.

2. Introduction and background epidemiology

The Lancefield group B beta-haemolytic streptococcus infection (*Streptococcus agalactiae*) is recognised as the most frequent cause of severe early-onset (less than 7 days of age) infection in newborn infants.[1] The GBS carriage rate varies among racial groups, with the highest rates in people of black African ancestry and the lowest in people of South Asian ancestry.

GBS is present in the bowel flora of 20–40% of adults (this is called 'colonisation'). People who are colonised are called 'carriers'. This includes pregnant women (there is no evidence that its carriage rate is specifically affected by pregnancy).

There remains controversy about the best strategy to prevent EOGBS disease. Surveys in 2015 demonstrated that there was a large variation in UK practice.[2] The incidence of EOGBS disease in the UK and Ireland in 2015 was 0.57/1000 births (517 cases), a significant increase in incidence since previous surveillance undertaken in 2000 (0.48/1000).[3] Of the cases, 22% had been born prematurely and overall, 35% had one or more of the following risk factors: a previous baby affected by GBS disease; GBS bacteriuria; a vaginal swab positive for GBS; or a maternal temperature of 38°C or greater in labour. Of the cases with discharge status, 7.4% were reported as having disability. A significant decline in case fatality rate was shown between the two surveillance periods: 10.6% to 5.2%, respectively.

Since 2002, the US guidelines[4] have advised that all pregnant women should be offered screening for GBS carriage at 35–37 weeks of gestation and those found to be colonised with GBS (or labouring before this time) should be offered intrapartum antibiotic prophylaxis (IAP), usually in the form of intravenous benzylpenicillin or ampicillin. IAP has been shown to significantly reduce the risk of culture-positive early-onset but not late-onset disease (occurring 7 or more days after birth). There is also indirect evidence of an impact on neonatal deaths. A longitudinal analysis of disease-related neonatal mortality in the USA showed a decline in mortality in the first week after birth, coinciding with the introduction of IAP.[5] A 2016 report from the USA shows a continuing fall in the incidence of GBS infection without any increase in deaths from other causes of neonatal disease.[6] A Cochrane review of three trials (all at high risk of bias) including 500 women concluded that IAP for colonised mothers reduced the incidence of EOGBS disease (relative risk 0.14; 95% CI 0.04–0.74) although the numbers of deaths were too small to assess the impact of the intervention on mortality.[7]

There have been no randomised studies addressing whether routine screening has had any impact on all-cause mortality. A positive antenatal screen will result in the recommendation of IAP which carries some risks for the mother and baby. These include anaphylaxis,[8] increased medicalisation of labour and the neonatal period, and possibly, infection with antibiotic-resistant organisms when broad-spectrum antibiotics, such as amoxicillin, are used for prophylaxis.[9,10] In the UK, most guidelines recommend that the first-line drug for GBS-specific IAP should be benzylpenicillin, also known as penicillin G. The UK National Screening Committee examined the issue of strategies for the prevention of EOGBS disease in 2016–17 and in March 2017 recommended that routine screening using bacteriological culture or near-patient testing techniques should not be introduced into UK practice.[11]

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2.1 *Role of vaccination to prevent EOGBS disease*

An effective vaccine given to pregnant women would be expected to induce high levels of GBS-specific immunoglobulin G in the woman and, via transplacental transfer, in her baby, resulting in protection against neonatal GBS disease (both EOGBS and late-onset GBS). Phase II trials of a trivalent GBS conjugate vaccine in pregnant women in South Africa and Malawi have demonstrated safety as well as efficient transplacental transfer of vaccine-specific antibodies.[11,12] Vaccine manufacturers are now developing pentavalent formulations (i.e. covering 5 of the 10 possible GBS serotypes) which would cover an estimated 96% of EOGBS cases in the UK. Another, or additional, potential mechanism of vaccine protection may be through reduction of maternal GBS colonisation and transmission to the baby. However, no clear effect of vaccination on colonisation was observed in the 2016 pregnancy trial with the trivalent conjugate vaccine.[11] Studies in the UK suggest that vaccination against GBS would be acceptable to pregnant women.[13,14]

3. Identification and assessment of evidence

This guideline was developed using standard methodology for developing RCOG Green-top Guidelines. The Cochrane Library (including the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects [DARE] and the Cochrane Central Register of Controlled Trials [CENTRAL]), EMBASE, MEDLINE and Trip were searched for relevant papers. The search was inclusive of all relevant articles published between January 2011 and October 2016. The databases were searched using the relevant Medical Subject Headings (MeSH) terms, including all subheadings and synonyms, and this was combined with a keyword search. Search terms included 'group B streptococcus', '*Streptococcus agalactiae*', 'group B streptococcus and pregnancy', 'streptococcal infections' and 'GBS bacteriuria'. The search was limited to studies on humans and papers in the English language. Relevant guidelines were also searched for using the same criteria in the National Guideline Clearinghouse and the National Institute for Health and Care Excellence (NICE) Evidence Search.

Where possible, recommendations are based on available evidence. Areas lacking evidence are highlighted and annotated as 'good practice points'. Further information about the assessment of evidence and the grading of recommendations may be found in Appendix I.

4. Information for women

4.1 *What information should women be given about GBS colonisation of the mother and the risk of neonatal infection, during pregnancy and after delivery?*

All pregnant women should be provided with an appropriate information leaflet. ✓

All pregnant women should be provided with an appropriate information leaflet, such as the RCOG patient information leaflet *Group B streptococcus (GBS) infection in newborn babies.*[15] Please see section 14 for more useful links and resources. Women should be offered information in a format that is accessible to them.

Evidence level 4

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5. Antenatal screening

5.1 Should all pregnant women be offered bacteriological screening for GBS?

Universal bacteriological screening is not recommended. D

The National Screening Committee[16] does not recommend universal bacteriological screening for GBS. Their view is that there is no clear evidence to show that testing for GBS routinely would do more good than harm. The reasons quoted are:

- Many women carry the bacteria and, in the majority of cases, their babies are born safely and without developing an infection.
- Screening women late in pregnancy cannot accurately predict which babies will develop GBS infection.
- No screening test is entirely accurate. Between 17% and 25% of women who have a positive swab at 35–37 weeks of gestation will be GBS negative at delivery. Between 5% and 7% of women who are GBS negative at 35–37 weeks of gestation will be GBS positive at delivery. Evidence level 4
- In addition, many of the babies who are severely affected from GBS infection are born prematurely, before the suggested time for screening.
- Giving all carriers of GBS IAP would mean that a very large number of women would receive treatment they do not need; this may increase adverse outcomes to mother and baby (see sections below).

This is why screening all women in pregnancy for GBS is not routinely offered in the UK. Some women choose to seek GBS testing outside the NHS. Providing the test is performed by an accredited laboratory, if the woman is found to be a carrier during the current pregnancy, IAP should be offered.

5.2 What are the clinical risk factors that affect the risk of GBS disease?

Clinicians should be aware of the clinical risk factors that place women at increased risk of having a baby with EOGBS disease. ✓

There are a number of clinical risk factors that appear to place women at increased risk of having a baby with EOGBS disease. These include:

- having a previous baby with GBS disease
- discovery of maternal GBS carriage through bacteriological investigation during pregnancy (for example, a urine infection or a swab taken to investigate a vaginal discharge)
- preterm birth
- prolonged rupture of membranes
- suspected maternal intrapartum infection, including suspected chorioamnionitis
- pyrexia.

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5.3 *Should women be offered IAP if GBS was detected in a previous pregnancy, irrespective of carrier status this pregnancy?*

Explain to women that the likelihood of maternal GBS carriage in this pregnancy is 50%. Discuss the options of IAP, or bacteriological testing in late pregnancy and the offer of IAP if still positive. B

If performed, bacteriological testing should ideally be carried out at 35–37 weeks of gestation or 3–5 weeks prior to the anticipated delivery date, e.g. 32–34 weeks of gestation for women with twins. C

Assuming that approximately 50% of women will be recurrent carriers, the risk of EOGBS disease should be approximately 2 to 2.5 times that quoted for the total population.[17–21] The risk of EOGBS disease in the baby in this circumstance is likely to be around 1 in 700 to 1 in 800.[3] At this risk level, some women would choose IAP and others would not. Bacteriological testing in this circumstance would help to refine the risk. A positive bacteriological test in this circumstance would indicate a risk of 1 in 400, but the risk would be 1 in 5000 if the mother is GBS negative. A significant number of mothers may therefore choose to avoid IAP if they test negative. Evidence level 1+

If bacteriological tests for GBS are to be performed in pregnancy they should ideally be performed at 35–37 weeks of gestation[22] in order to determine carriage status close to delivery. There is no evidence to support the practice of varying the timing of screening. However, in women where preterm delivery is anticipated, earlier testing is justified. Evidence level 2+

5.4 *Should women with a previous baby affected by GBS disease be offered IAP irrespective of carrier status this pregnancy?*

IAP should be offered to women with a previous baby with early- or late-onset GBS disease. D

The proportion of term pregnant women with a previous baby affected by EOGBS is assumed to be 0.08%, based on a consensus estimate from a UK modelling study.[23] Mothers who have had a previous baby affected by early- or late-onset GBS are at increased chance of another affected baby compared with women of similar carrier status who have not had an affected baby. The reasons for this increased risk are not clear but may indicate persistence of carriage of a virulent strain of GBS or a deficient immune response.[24–26] In view of this potentially increased risk, and the possibility of false-negative antenatal testing, we recommend giving IAP in such cases and maternal bacteriological tests are not recommended. Evidence level 3

5.5 *What screening tests (if any) should be offered if a woman requests testing for carrier status?*

A maternal request is not an indication for bacteriological screening. D

The National Screening Committee does not recommend universal bacteriological screening for GBS. Evidence level 4

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6. Antenatal care

6.1 *How should GBS bacteriuria in the current pregnancy be managed?*

Clinicians should offer IAP to women with GBS bacteriuria identified during the current pregnancy. C

Women with GBS urinary tract infection (growth of greater than 10^5 cfu/ml) during pregnancy should receive appropriate treatment at the time of diagnosis as well as IAP. C

GBS bacteriuria is associated with a higher risk of chorioamnionitis and neonatal disease although it is not possible to quantify these risks accurately. Women with GBS bacteriuria should be offered IAP. Women with GBS urinary tract infection (growth of greater than 10^5 cfu/ml) during pregnancy should receive appropriate treatment at the time of diagnosis as well as IAP.[27] Evidence level 3

6.2 *Should women be treated before the onset of labour if GBS carriage is detected incidentally earlier in the pregnancy?*

Antenatal treatment is not recommended for GBS cultured from a vaginal or rectal swab. C

Antenatal treatment for vaginal or rectal colonisation does not reduce the likelihood of GBS colonisation at the time of delivery[28] and so is not indicated in this situation. Instead, IAP should be offered to GBS-colonised women (see section 6.3). Evidence level 2+

6.3 *Should the management differ if the detection of GBS is incidental or following intentional testing, and if so, how?*

Where GBS carriage is detected incidentally or by intentional testing, women should be offered IAP. ✓

There is no evidence to support different management strategies based on how GBS carriage was detected.

6.4 *Should being a GBS carrier influence the method of induction?*

Method of induction should not vary according to GBS carrier status. ✓

There is no evidence to suggest that different induction methods increase the risk of EOGBS disease. If indicated, intravenous IAP should be commenced once a diagnosis of established labour has been made following induction.

6.5 *Is being a GBS carrier a contraindication to membrane sweeping?*

Membrane sweeping is not contraindicated in women who are carriers of GBS. D

There is evidence that membrane sweeping does not increase the risk of EOGBS disease.[29] Evidence level 2–

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6.6 *How should planned caesarean section in women with known GBS colonisation be managed?*

Antibiotic prophylaxis specific for GBS is not required for women undergoing planned caesarean section in the absence of labour and with intact membranes. C

All women having caesarean section should receive broad-spectrum antibiotic prophylaxis in line with the NICE clinical guideline *Caesarean section*.[30] Women undergoing planned caesarean delivery in the absence of labour or membrane rupture do not require additional penicillin antibiotic prophylaxis specifically for GBS, regardless of GBS colonisation status. The risk of neonatal EOGBS disease is extremely low in this circumstance.

Women who are known GBS carriers who are to be delivered by caesarean section after spontaneous rupture of membranes should be offered IAP and delivered by category 2 or 3 caesarean depending on other clinical findings.[31] Evidence level 3

7. Management of term labour (including rupture of membranes) to reduce the risk of EOGBS disease

7.1 *How should rupture of membranes in a woman at term (37^{+0} weeks of gestation) with known or unknown GBS carrier status be managed?*

Women who are known GBS carriers should be offered immediate IAP and induction of labour as soon as reasonably possible. C

In women where the carrier status is negative or unknown, offer induction of labour immediately or expectant management up to 24 hours. Beyond 24 hours, induction of labour is appropriate. A

If known to be colonised with GBS, women should be offered immediate IAP because of the increased risk of EOGBS disease with prolonged rupture of membranes.[32] Evidence level 2+

As recommended in NICE clinical guideline 70[33] women should be offered induction of labour immediately or up to 24 hours after spontaneous rupture of membranes with unknown carrier status.[32] Evidence level 1+

7.2 *How should labour in a woman with a temperature of 38°C or greater and without known GBS colonisation be managed?*

Women who are pyrexial (38°C or greater) in labour should be offered a broad-spectrum antibiotic regimen which should cover GBS in line with local microbiology sensitivities. C

Intrapartum pyrexia (38°C or greater) is associated with a risk of EOGBS disease of 5.3 per 1000 (versus a background risk of 0.6 per 1000).[34]

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In view of this increased risk of EOGBS, IAP should be offered in the presence of maternal pyrexia. Since a raised temperature can indicate chorioamnionitis, a broad-spectrum antibiotic, rather than penicillin G, is recommended in this situation. The antibiotic regimen of choice will depend on local microbiology guidance; intravenous amoxicillin 2 g every 6 hours (or intravenous cefuroxime 1.5 g every 6 hours in women with a nonanaphylactic reaction to penicillin) is acceptable in this context.[35]

Evidence level 3

7.3 *How should preterm labour be managed in women without known GBS colonisation?*

IAP is recommended for women in confirmed preterm labour. D

IAP is not recommended for women not in labour and having a preterm planned caesarean section with intact membranes. D

The proportion of women giving birth preterm in the UK is 8.2%.[36] More women present in **threatened** preterm labour than deliver preterm. The risk of EOGBS disease in the infants of those women who deliver preterm is estimated to be 2.3 per 1000.[23] The risk of GBS infection is higher with preterm delivery and the mortality rate from infection is increased (20–30% versus 2–3% at term).[37,38] In the 2015 British Paediatric Surveillance Unit national UK surveillance study, the mortality rate in preterm infants at 33 weeks of gestation or less was 27% versus 2.7% at term.[39] For this reason, IAP is recommended for women in **confirmed** preterm labour. However, IAP is not recommended for women having preterm planned caesarean section with intact membranes.

Evidence level 4

7.4 *Is there a role for polymerase chain reaction or other near-patient testing at the onset of labour?*

Polymerase chain reaction or other near-patient testing at the onset of labour is not recommended. C

The evidence does not suggest that using polymerase chain reaction technology for near-patient testing is feasible in UK maternity labour ward settings.[40] The technology for near-patient testing continues to improve and it is possible that this may confer benefits in the future. An ongoing cluster randomised trial is testing whether the use of near-patient testing in labour can reduce the use of IAP in women who present with clinical risk factors who would be eligible for IAP.

Evidence level 2+

7.5 *Can GBS-positive women have a water birth?*

Birth in a pool is not contraindicated if the woman is a known GBS carrier provided she is offered appropriate IAP. D

The evidence suggests that water birth is not contraindicated for GBS-positive women who have been offered the appropriate IAP.[41–43]

Evidence level 3

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8. Management of preterm labour (including rupture of membranes) to reduce the risk of EOGBS disease

8.1 Women with preterm rupture of membranes

8.1.1 How should known or unknown GBS carrier status be managed in women with preterm prelabour rupture of membranes?

Bacteriological testing for GBS carriage is not recommended for women with preterm rupture of membranes. IAP should be given once labour is confirmed or induced irrespective of GBS status. D

For those with evidence of colonisation in the current pregnancy or in previous pregnancies, the perinatal risks associated with preterm delivery at less than 34^{+0} weeks of gestation are likely to outweigh the risk of perinatal infection. For those at more than 34^{+0} weeks of gestation it may be beneficial to expedite delivery if a woman is a known GBS carrier. D

There is no evidence that treating GBS colonisation before labour is beneficial.[44–46] Therefore, a prelabour-positive GBS culture does not change management in pregnancies with a gestation of less than 34^{+0} weeks because the high morbidity associated with early preterm birth means that early delivery is not indicated unless there are overt signs of infection. The risk of GBS infection is higher with preterm delivery and the mortality rate from infection is increased (20–30% versus 2–3% at term)[37,38] and this therefore justifies IAP in all cases of preterm labour.

The NICE guideline *Preterm labour and birth*[47] recommends that all women with preterm prelabour rupture of the membranes should be offered oral erythromycin 250 mg, 4 times a day for a maximum of 10 days or until the woman is in established labour (whichever is sooner). Oral penicillin should be considered for the same duration in women who cannot tolerate erythromycin or in whom erythromycin is contraindicated. Evidence level 4

A large multicentre randomised controlled trial (RCT) of elective delivery at 34–36 weeks of gestation for preterm spontaneous rupture of membranes versus conservative management[48] has demonstrated no significant differences in neonatal disease, morbidity or mortality. As a result, there is no indication to prefer one form of management over the other at this gestational age although IAP should be given once labour starts. There may be disadvantages with conservative management beyond 34^{+0} weeks of gestation in the presence of known GBS colonisation and in this group, early intervention may be preferable.[49]

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9. Bacteriological considerations

Public Health England has published a standard for the detection of GBS carriage.[50]

9.1 What are the appropriate swabs if testing for carrier status is to be undertaken?

When testing for GBS carrier status, a swab should be taken from the lower vagina and the anorectum. A single swab (vagina then anorectum) or two different swabs can be used. **D**

Public Health England has published a standard for the detection of GBS carriage.[50] The standard notes that optimum yield will be achieved with swabs obtained from the lower vagina and the anorectum. A single swab for both sites of collection is rational but two different swabs can be used. The swabs may be rayon or dacron, fibre or flocked, and may be collected by the physician or other qualified caregiver, or by the woman with appropriate instruction. These tests are described as enriched culture medium tests. Evidence level 4

9.2 How quickly should the swabs be transported to the laboratory, in what medium and at what temperature?

After collection, swabs should be placed in a non-nutrient transport medium, such as Amies or Stuart. Specimens should be transported and processed as soon as possible. If processing is delayed, specimens should be refrigerated. **D**

GBS isolates can remain viable in transport media for several days at room temperature. However, the recovery of isolates declines over 1–4 days, especially at elevated temperatures, which can lead to false-negative results. When feasible, specimens should be refrigerated before processing.[4] Evidence level 4

9.3 What culture medium should be used if testing for GBS carriage is to be undertaken?

Enriched culture medium tests are recommended. The clinician should indicate that the swab is being taken for GBS. **D**

The most widely used enriched culture medium is Todd-Hewitt broth with nalidixic acid and colistin (e.g. Lim broth), or nalidixic acid and gentamicin further subcultured on a blood agar plate. Several options are available for the subculture of an enriched culture medium for isolation of GBS, including selective and chromogenic agar.[4] Evidence level 4

9.4 Which antibiotic should be used for IAP?

For women who have agreed to IAP, benzylpenicillin should be administered. Once commenced, treatment should be given regularly until delivery. **B**

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It is recommended that 3 g intravenous benzylpenicillin be given as soon as possible after the onset of labour and 1.5 g 4 hourly until delivery. To optimise the efficacy of IAP, the first dose should be given at least 4 hours prior to delivery. There is evidence that benzylpenicillin levels in cord blood exceed the minimum inhibitory concentration for GBS as early as 1 hour after maternal administration[51] but it is not known how this relates to neonatal colonisation or disease. There is also evidence that giving penicillin for 2 hours before delivery reduces neonatal colonisation[52,53] but evidence from 2013[54] suggests that 4 hours of penicillin is more effective than 2 hours at reducing the risk of EOGBS disease. Amoxicillin is an alternative but the Cochrane review[7] found no difference between amoxicillin and benzylpenicillin and thus, the narrower spectrum antibiotic is preferred.

Evidence level 2+

9.5 *Which antibiotic should be used in women with known or suspected penicillin allergy?*

Provided a woman has not had severe allergy to penicillin, a cephalosporin should be used. If there is any evidence of severe allergy to penicillin, vancomycin should be used. ✓

The antibiotic chosen will depend on the confidence of the diagnosis of penicillin allergy and the severity of penicillin allergy. If the history suggests that the reaction described is not likely to be allergic in nature (e.g. vomiting only) then penicillin should be given. If the history suggests an allergy to beta-lactams, but one that is not severe (i.e. no anaphylaxis, angioedema, respiratory distress or urticaria), then a cephalosporin can be administered intravenously (e.g. cefuroxime, 1.5 g loading dose followed by 750 mg every 8 hours). If the allergy to beta-lactams is severe then intravenous vancomycin (1 g every 12 hours) is recommended.[4]

Clindamycin can no longer be recommended as the current resistance rate in the UK is 16%.[39]

Evidence level 4

9.6 *How should known GBS colonisation in women who decline IAP be managed?*

Women with known GBS colonisation who decline IAP should be advised that the baby should be very closely monitored for 12 hours after birth, and discouraged from seeking very early discharge from the maternity hospital. ✓

Women should be made aware that the risk of the baby developing EOGBS infection is higher than if they had received IAP. The overall risk remains low. The baby will require clinical evaluation at birth and monitoring of vital signs for 12 hours.[55]

Evidence level 4

9.7 *What are the adverse effects of IAP (maternal anaphylaxis, altered neonatal bowel flora and abnormal child development)?*

Clinicians should be aware of the potential adverse effects of IAP. C

A positive antenatal screen will result in the recommendation of IAP, which may carry some risks for mother and baby. A UK Obstetric Surveillance System study (2012–2015)[56] identified 37 cases of maternal anaphylaxis over 3 years (1.6/100 000 maternities), around 50% of which were associated with the administration of antibiotics (0.8/100 000 maternities) although it is not known whether any were given as IAP.

Evidence level 3

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A number of studies have shown an effect of IAP on neonatal bowel flora, for example, causing reductions in colonisation with lactobacilli or bifidobacterium, but these findings have not been consistent across all studies.[57–61]

Evidence level 2++

Changes in the neonatal bowel microbiome have been linked to a number of later effects in the child, including allergy, and obesity and diabetes.[62–64] However, these risks remain theoretical.

Evidence level 2+

There are no studies showing that IAP adversely affects child development. The ORACLE I trial showed that oral erythromycin or co-amoxiclav given to pregnant women with preterm prelabour rupture of the membranes for up to 10 days was not associated with any long-term adverse outcomes.[65] However, the ORACLE II trial showed that oral erythromycin given to pregnant women in spontaneous preterm labour with intact membranes for up to 10 days was associated with long-term functional impairment in children (odds ratio 1.18, 95% CI 1.02–1.37), and both oral erythromycin (odds ratio 1.93, 95% CI 1.21–3.09) and co-amoxiclav (odds ratio 1.69, 95% CI 1.07–2.67) were associated with cerebral palsy at the age of 7 years.[66] However, this was a different scenario to that of IAP. Moreover, at the age of 11 years, no effect of these antibiotics given in either spontaneous preterm labour or prelabour rupture of membranes was found on continuous outcome scores, contextual value added measure (a measure of education progress), or on criterion-referenced attainment or identified special needs.[67]

Evidence level 4

10. Should vaginal cleansing be performed in labour and does this differ according to GBS carrier status?

There is no evidence that intrapartum vaginal cleansing will reduce the risk of neonatal GBS disease.

C

Although vaginal cleansing with chlorhexidine has been shown to reduce the risk of neonatal GBS colonisation, there is no evidence to show that this has any impact on EOGBS disease.[68]

Evidence level 3

11. How should a newborn baby be managed?

11.1 *If there have been any concerns about early-onset neonatal infection, what signs should prompt parents and carers to seek medical advice?*

Parents and carers should seek urgent medical advice if they are concerned that the baby:

D

- **is showing abnormal behaviour (for example, inconsolable crying or listlessness), or**
- **is unusually floppy, or**
- **has developed difficulties with feeding or with tolerating feeds, or**
- **has an abnormal temperature unexplained by environmental factors (lower than 36°C or higher than 38°C), or**
- **has rapid breathing, or**
- **has a change in skin colour.**

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The NICE clinical guideline *Neonatal infection (early onset): antibiotics for prevention and treatment*,[55] outlines symptoms and signs in the neonate that should prompt urgent medical advice. Parents and carers should be aware of these if there have been any concerns about early-onset neonatal infection before a baby is discharged.

Evidence level 4

11.2 *How should term babies whose mothers have received adequate IAP be managed?*

Term babies who are clinically well at birth and whose mothers have received IAP for prevention of EOGBS disease more than 4 hours before delivery do not require special observation. ✓

The babies of women who have received broad-spectrum antibiotics during labour for indications other than GBS prophylaxis may require investigation and treatment as per the NICE clinical guideline on early-onset neonatal infection. ✓

Given that adequate IAP reduces the risk of EOGBS disease to a level approaching that of the general population it seems reasonable to manage these babies as low risk.[7]

Evidence level 4

11.3 *How should well babies at risk of EOGBS disease whose mothers have not received adequate IAP be monitored?*

Well babies should be evaluated at birth for clinical indicators of neonatal infection and have their vital signs checked at 0, 1 and 2 hours, and then 2 hourly until 12 hours. ✓

Two studies[52,69] have shown that 90% of infants who are diagnosed with early-onset infection will display signs by 12 hours.[55]

Evidence level 4

11.4 *Should postnatal antibiotic prophylaxis be given to low-risk term babies?*

Postnatal antibiotic prophylaxis is not recommended for asymptomatic term infants without known antenatal risk factors. C

The incidence of EOGBS disease in asymptomatic term infants without known antenatal risk factors in the UK is estimated at 0.2 cases/1000 births.[70] No RCT has investigated treatment in this group. If postnatal antibiotic treatment was completely effective and there were no adverse effects, 5000 infants would need to be treated to prevent a single case and at least 80 000 infants would have to be treated to prevent a single death from EOGBS disease. Routine postnatal antibiotic prophylaxis is not recommended.

Evidence level 3

11.5 *How should a baby with clinical signs of EOGBS disease be managed?*

Babies with clinical signs of EOGBS disease should be treated with penicillin and gentamicin within an hour of the decision to treat. ✓

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The NICE guideline on early-onset neonatal infection[55] contains a list of clinical indicators of neonatal infection and is provided as an appendix in this guideline (see Appendix II). Clinicians caring for babies with clinical signs of EOGBS disease should be aware of these factors. Appropriate investigations should be performed in line with the NICE guidance,[55] and treatment with intravenous penicillin and gentamicin commenced without delay and without awaiting the results of investigations.

Evidence level 4

11.6 How should the baby of a mother who has had a previous baby with GBS disease be managed?

Babies should be evaluated at birth for clinical indicators of neonatal infection and have their vital signs checked at 0, 1 and 2 hours, and then 2 hourly until 12 hours. ✓

The baby of a mother who has had a previous baby with GBS disease is believed to be at increased risk of EOGBS although it is not possible to estimate the size of this risk.

Mothers who have had a previous baby with GBS disease will be offered IAP. Following careful clinical assessment the baby's vital signs and clinical condition should be monitored closely for at least 12 hours (see NICE clinical guideline 149).[55]

Evidence level 4

Although some clinicians prefer to obtain blood cultures and treat the baby with intravenous penicillin, and then stop the antibiotics at 36 hours if the cultures are negative, there is no evidence that this is necessary.

11.7 What advice should be given to women regarding breastfeeding?

Breastfeeding should be encouraged irrespective of GBS status. ✓

There is no evidence to discourage breastfeeding where there are concerns regarding the possible risk of transmission of GBS disease.

12. Recommendations for future research

- Cluster randomised trial of screening for GBS carriage with the offer of IAP for carriers to investigate the benefits and harms of a bacteriological screening programme.
- Studies of the virulence of specific strains identified using genetic markers and of serological correlates of protection.
- What is the long-term prognosis and associated costs for infants who survive EOGBS disease?
- What is the safety, immunogenicity and efficacy of a GBS vaccine in pregnant women?
- Can serocorrelates of protection against GBS be defined and used to facilitate the licensure of a GBS vaccine without the need for large-scale prelicensure efficacy trials in pregnant women?

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13. Auditable topics

- Proportion of pregnant women with the following indications for IAP who actually received IAP (100%):
  - preterm labour
  - previous invasive GBS disease
  - known GBS carrier (however detected)
  - GBS bacteriuria or GBS urinary tract infection in current pregnancy.
- Proportion of women who are pyrexial in labour who are offered appropriate antibiotics, including antibiotic for preventing EOGBS (100%).
- Proportion of pregnant women who were colonised in a previous pregnancy who are offered testing and/or IAP (100%).
- Proportion of pregnant women given high-quality patient information (100%).
- Percentage of professionals with knowledge and understanding of GBS carriage and EOGBS disease (100%).

14. Useful links and support groups

- Royal College of Obstetricians and Gynaecologists. *Group B streptococcus (GBS) infection in newborn babies. Information for you*. London: RCOG; 2017 [https://www.rcog.org.uk/en/patients/patient-leaflets/group-b-streptococcus-gbs-infection-in-newborn-babies/].
- Free information materials both printed and online are available from Group B Strep Support [www.gbss.org.uk; *Telephone: 01444 416176*].

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Appendix I: Explanation of guidelines and evidence levels

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No.1 *Development of RCOG Green-top Guidelines* (available on the RCOG website at www.rcog.org.uk/green-top-development). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels

1++	High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias
1–	Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

A	At least one meta-analysis, systematic review or RCT rated as 1++, and directly applicable to the target population; or A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+ directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

Good practice points

✓	Recommended best practice based on the clinical experience of the guideline development group

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Appendix II: Clinical indicators of possible early-onset neonatal infection (observations and events in the baby), including 'red flags'

Clinical indicator	Red flag
Altered behaviour or responsiveness	
Altered muscle tone (for example, floppiness)	
Feeding difficulties (for example, feed refusal)	
Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension	
Abnormal heart rate (bradycardia or tachycardia)	
Sign of respiratory distress	
Respiratory distress starting more than 4 hours after birth	**Yes**
Hypoxia (for example, central cyanosis or reduced oxygen saturation level)	
Jaundice within 24 hours of birth	
Apnoea	
Signs of neonatal encephalopathy	
Seizures	**Yes**
Need for cardio-pulmonary resuscitation	
Need for mechanical ventilation in a preterm baby	
Need for mechanical ventilation in a term baby	**Yes**
Persistent fetal circulation (persistent pulmonary hypertension)	
Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors	
Signs of shock	**Yes**
Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation (International Normalised Ratio greater than 2.0)	
Oliguria persisting beyond 24 hours after birth	
Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)	
Metabolic acidosis (base deficit of 10 mmol/litre or greater)	
Local signs of infection (for example, affecting the skin or eye)	

National Institute for Health and Clinical Excellence (2012) Neonatal infection (early onset): antibiotics for prevention and treatment. Available from: [https://www.nice.org.uk/guidance/cg149] NICE guidance is prepared for the National Health Service in England, and is subject to regular review and may be updated or withdrawn. NICE has not checked the use of its content in this guideline to confirm that it accurately reflects the NICE publication from which it is taken.

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This guideline was produced on behalf of the Royal College of Obstetricians and Gynaecologists by:
Dr RG Hughes FRCOG, Edinburgh; Professor P Brocklehurst FRCOG, Birmingham; Professor PJ Steer FRCOG, London; Professor P Heath, St George's University London; Professor BM Stenson, Royal Infirmary of Edinburgh

and peer reviewed by:
British Infection Association; Professor L Chappell MRCOG, London; Dr M Eogan MD FRCPI MRCOG, Rotunda Hospital, Dublin, Ireland; Dr R Fernando, President of the Obstetric Anaesthetists' Association, London; Dr G Gopal Rao FRCPath, Northwick Park Hospital, London; Dr J Gray FRCPath, Birmingham Children's Hospital; Group B Strep Support; Dr T Kay FRCOG, Exeter; Professor S Kenyon, University of Birmingham; RCOG Women's Network; Royal College of Paediatrics and Child Health; Dr A Soe FRCPCH, Medway

Committee lead reviewers were: Dr A Thomson MRCOG, Paisley; and Dr B A Magowan FRCOG, Melrose

The chairs of the Guidelines Committee were: Dr M Gupta MRCOG, London; and Dr AJ Thomson MRCOG, Paisley

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The guideline will be considered for update 3 years after publication, with an intermediate assessment of the need to update 2 years after publication.

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